REMARKS

Claims 145-147 and 149-154 are pending in the present application.

Priority

Applicants respectfully disagree with the Examiner's position with respect to the priority date. However, in an effort to expedite prosecution and for examination purposes only, Applicants rely on the filing date of the instant application for the pending claims. Applicants reserve the right to establish the benefit of an earlier priority date at a later time.

Rejection under 35 U.S.C. § 112

The Examiner has rejected claims 145-147 and 149-154 under 35. U.S.C. § 112, first paragraph as allegedly failing to adequately describe the invention. Specifically, the Examiner asserts that "the instant application does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand is not administered to the transplant recipient," as broadly claimed in the instant claims" (see Office Action, page 2).

Applicants respectfully traverse the rejection. Applicants note that if alternative elements are positively recited in the specification, they may be explicitly excluded in the claims (See MPEP 2173.05(i)). Applicants further note that the inventors are permitted to exclude old or obvious species from the claims if the Applicants literally and positively disclosed these species in their specification, such that "[the] specification, having described the whole, necessarily described the part remaining." (See *In Re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977).

Applicants point to the Examiner's statement that "the instant USSN 09/501,102 provides for the recitation of "anti-CD40 pathway inhibitors (e.g. anti-CD40 antibodies, anti-CD40 ligand antibodies and small molecule inhibitors of the CD40 pathway" as another drug that can be administered with B7-1-/B7-2-specific antibodies"" (see pending Office Action, page 2) as support for the positive recitation of administration of inhibitors of CD40 or CD40 ligand in combination with B7-1-/B7-2-specific immunoglobulins. According to MPEP 2173.05(i), by excluding what was positively recited in the specification, the inventors are thus not claiming new matter. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

The Examiner also asserts that the inventors' "disclosure of certain "inhibitors of CD40 or CD40 ligand" (e.g. anti-CD40 antibodies, anti-CD40 ligand antibodies) does not provide sufficient written description for certain "inhibitors of CD40 or CD40 ligand", as currently claimed" (see pending Office Action, page 3).

Applicants respectfully traverse the rejection. One of skill in the art would understand that Applicants were in possession of "inhibitors of CD40 or CD40 ligand," including anti-CD40 antibodies and anti-CD40 ligand antibodies. Issued patents in the art, for example, de Boer et al. in U.S. Patent 5,677,165 issued on Oct. 14, 1997 and Armitage et al. in U.S. Patent 5,961,974 issued on Oct. 5, 1999 demonstrate that antibody inhibitors of both CD40 and CD40 ligand, respectively, were generally known at the time the instant application was filed. In addition, such antibodies have been shown to disrupt the CD40-CD40 ligand costimulatory interaction (see, e.g. as exemplified in Armitage et al., U.S. Patent 5,961,974 filed May 24, 1994, in Fanslow, III et al., U.S. Patent 5,801,227 filed Sept. 8, 1995 and the like). These examples, known in the art at the time the instant application was filed, provide a sufficient number of species to represent the entire genus as currently claimed. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 102

The Examiner has rejected claims 145-147 and 154 under 35 U.S.C. § 102(e) as allegedly being anticipated by Freeman et al. (U.S. Patent No. 6,605,279). The Examiner asserts that "Freeman et al. teach methods of downregulating or suppressing T cell mediated immune responses, including the use of B7-1-specific and B7-2-specific antibodies in conjunction with other immunomodulating reagents, such as cyclosporine or FK506, including its usefulness in situations of tissue and organ transplantation, as well as GVHD" (see pending Office Action, page 7). Applicants respectfully traverse the rejection.

Freeman et al. does not teach or suggest a method wherein an immunoglobulin specific to B7-1 and an immunoglobulin specific to B7-2 are administered to a transplant recipient **wherein an inhibitor to CD40 or CD40 ligand is specifically not administered to the transplant recipient**. In fact, Freeman et al. does not even mention CD40 or CD40 ligand. Freeman et al. therefore does not teach or suggest the elements of the pending claims, and thus does not

anticipate or render obvious the claimed invention. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected claims 145-147 and 149-154 under 35 U.S.C. § 103(a) as being unpatentable over Freeman et al. (U.S. Patent No. 6,605,279) in view of de Boer et al. (U.S. Patent No. 5,757,034). Specifically, the Examiner states that claims 145-147 and 149-154 are "unpatentable over Freeman et al. (U.S. Patent No. 6,605,279) in view of the well known use of immunosuppressives, such as cyclosporin, FK506 and rapamycin and effective therapeutic antibody dosages in transplantation therapeutic regimens at the time the invention was made, as taught by de Boer et al. (U.S. Patent No. 5,757,034)" (see pending Office Action, page 8). Applicants respectfully traverse the rejection.

Applicants respectfully remind the Examiner that the references must be viewed as a whole and must suggest the desirability of the claimed invention without the benefit of impermissible hindsight reconstruction afforded by the claimed invention. Furthermore, in order "[t]o establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." MPEP §2143.03 citing *In re* Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

As set forth above, Freeman et al. does not teach or suggest a method wherein an immunoglobulin specific to B7-1 and an immunoglobulin specific to B7-2 are administered to a transplant recipient **wherein an inhibitor to CD40 or CD40 ligand is specifically not administered to the transplant recipient**. Likewise, de Boer et al. does not teach or suggest a method wherein an immunoglobulin specific to B7-1 and an immunoglobulin specific to B7-2 are administered to a transplant recipient **wherein an inhibitor to CD40 or CD40 ligand is specifically not administered to the transplant recipient.** Accordingly, the cited references, either alone or in combination, fail to teach or suggest the currently claimed methods.

In addition, neither Freeman et al., nor de Boer et al., either alone or in combination, teach or suggest administration of therapeutically effective amounts of the therapeutic compositions, wherein amounts of effective dosages are administered for periods of time necessary to achieve the desired results as claimed. As pointed out by the Examiner, "Freeman et al. differs from the claimed methods by not disclosing…effective therapeutic antibody dosages

in transplantation therapeutic regimens at the time the invention was made." (see pending Office Action, page 8). De Boer et al. discloses generic therapeutic amounts and modes of administration (e.g., see column 16, paragraph 5). Moreover, de Boer et al. do not provide any examples demonstrating that such generic therapeutic regimens would be therapeutically effective for the claimed purpose of treating a transplant recipient or preventing transplant rejection. In contrast, the instant application discloses effective therapeutic amounts and time courses for administration that have led to decreases and even complete prevention of immune responses in transplant subjects (see page 42, lines 16-18 and Examples 22 and 23). Such effective therapeutic regimens are not taught or suggested by Freeman et al. or de Boer et al. Freeman et al. and de Boer et al., therefore, neither teach nor suggest, either alone or in combination, effective therapeutic dosages in transplantation therapeutic regimens and therefore are not enabling for the teachings that the Examiner contends the references disclose. Any additional teaching regarding the use of B7-specific antibodies in combination with immunosuppressive agents does not rectify the lack of teaching of the claimed therapeutic methods by Freeman et al. and de Boer et al. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable consideration of the application is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at (617) 832-1264. If any fees are due, the Commissioner is hereby authorized to credit any overpayment or charge any deficiencies to Deposit Account No. **Deposit Account No. 06-1448, WYS-004.01.**

Respectfully submitted,

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